L4
1-12
APTS
OWN WORK

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L1 STRUCTURE UPLOADED

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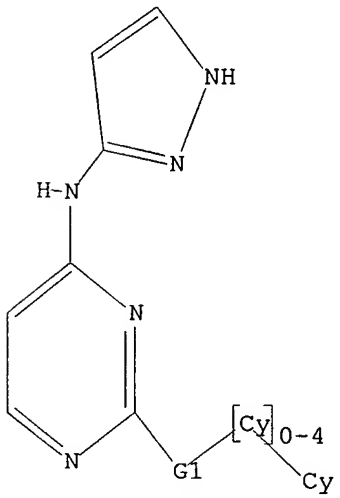
L1 STR



G1 C,O,S,N,Cb,Ak

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 43 TO ITERATE

100.0% PROCESSED 43 ITERATIONS 16 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:	ONLINE	**COMPLETE**
	BATCH	**COMPLETE**
PROJECTED ITERATIONS:	467 TO	1253
PROJECTED ANSWERS:	80 TO	560

L2 16 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 16:46:26 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 913 TO ITERATE

100.0% PROCESSED 913 ITERATIONS 243 ANSWERS
SEARCH TIME: 00.00.01

L3 243 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 148.15 148.36

FILE 'CAPLUS' ENTERED AT 16:46:32 ON 28 MAR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 28 Mar 2003 VOL 138 ISS 14
FILE LAST UPDATED: 27 Mar 2003 (20030327/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4 15 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:615605 CAPLUS
DOCUMENT NUMBER: 137:169539
TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer, diabetes, and Alzheimer's disease
INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Golec, Julian M. C.; Miller, Andrew; Knegtel, Ronald
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 335 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062789	A1	20020815	WO 2001-US51031	20011219
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US 2003036543	A1	20030220	US 2001-25164	20011219
US 2003055068	A1	20030320	US 2001-26967	20011219
US 2003004164	A1	20030102	US 2001-34683	20011220
US 2003022885	A1	20030130	US 2001-34019	20011220

PRIORITY APPLN. INFO.: US 2000-257887P P 20001221
US 2001-286949P P 20010427

OTHER SOURCE(S): MARPAT 137:169539
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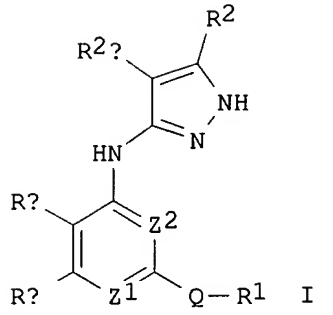

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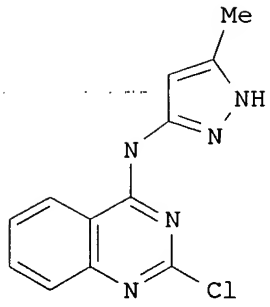

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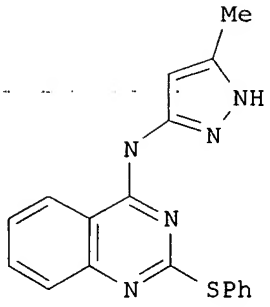
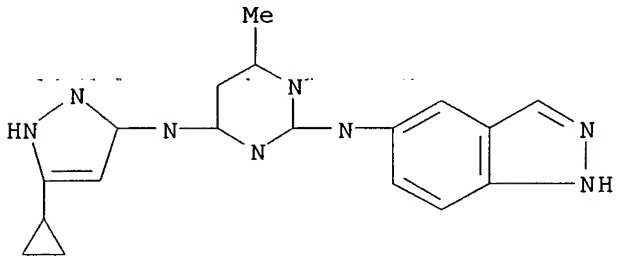


III

AB 285 Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1 of Z1 and Z2 = N; Rx and Ry = independently TR3 or LZR3; or C2RxRy = (un)substituted fused (hetero)cycle; Q = NR4, O, S, C(R6')2, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, or carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4, CO, CONH, NHCO, SO2, SO2NH, NHSO2, CO2, OCO, OCONH, or NHCO2, with provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6, NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a = independently R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un)substituted aliph., (hetero)aryl, or heterocyclyl; R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2, CONR6, C(R6)2O, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or C(R6)2NR6CONR6; R6, R6', R7 = independently H or aliph.; or N(R6)2 or N(R7)2 = independently heterocyclyl or heteroaryl; or C(R6')2 = carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepd. However, the claims pertain only to 3-(2-amino-4-pyrimidinylamino)-1H-pyrazoles, i.e. Z1 = Z2 = N, and Q = NH. I are protein kinase inhibitors, esp. of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 .mu.M: GSK-3.beta. (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases assocd. with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT **446881-34-1P**, N4-(5-Cyclopropyl-1H-pyrazol-3-yl)-N2-(1H-indazol-5-

yl)-6-methylpyrimidine-2,4-diamine **446881-35-2P**,
N2-Benzothiazol-6-yl-N4-(5-cyclopropyl-1H-pyrazol-3-yl)-6-methylpyrimidine-2,4-diamine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)
RN 446881-34-1 CAPLUS
CN 2,4-Pyrimidinediamine, N4-(5-cyclopropyl-1H-pyrazol-3-yl)-N2-1H-indazol-5-yl-6-methyl- (9CI) (CA INDEX NAME)



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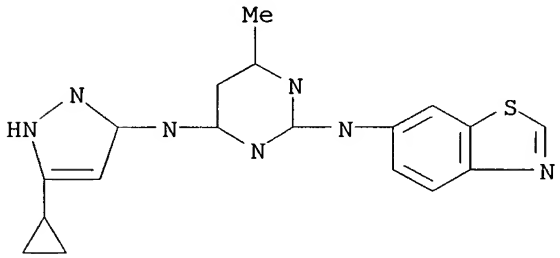

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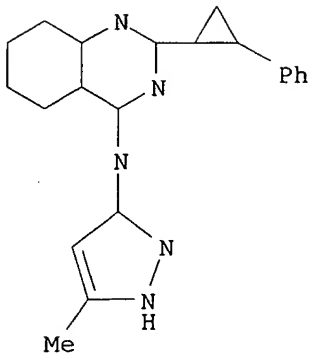
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of (pyrimidinylamino)pyrazoles as



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REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:575069 CAPLUS
DOCUMENT NUMBER: 137:109292
TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer, diabetes, and Alzheimer's disease
INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Davies, Robert; Golec, Julian; Kay, David; Knegtel, Ronald; Patel, Sanjay
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 337 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059111	A2	20020801	WO 2001-US51120	20011219
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WO 2002066461	A1	20020829	WO 2001-US49139	20011219
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WO 2002068415 A1 20020906 WO 2001-US50312 20011219

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US 2003004161 A1 20030102 US 2001-26975 20011219

US 2003036543 A1 20030220 US 2001-25164 20011219

US 2003055068 A1 20030320 US 2001-26967 20011219

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US 2003022885 A1 20030130 US 2001-34019 20011220

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US 2001-286949P P 20010427

OTHER SOURCE(S): MARPAT 137:109292

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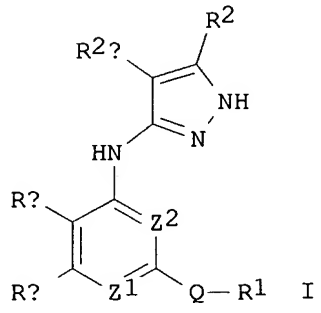

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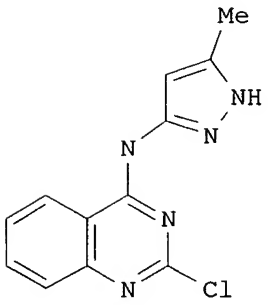

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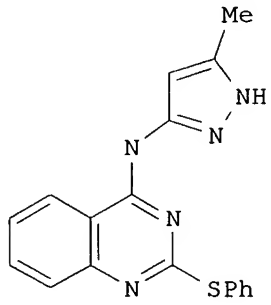

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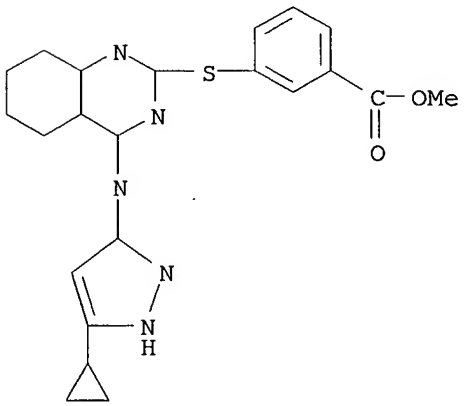
AB Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1 of Z1 and Z2 = N; Rx and Ry = independently TR3 or LZR3; or C2RxRy = (un)substituted fused (hetero)cycle; Q = NR4, O, S, C(6a)2, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, or

carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4, CO, CONH, NHCO, SO2, SO2NH, NHSO2, CO2, OCO, OCONH, or NHCO2, with provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6, NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a = independently R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un)substituted aliph., (hetero)aryl, or heterocyclyl; R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2, CONR6, C(R6)2O, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or C(R6)2NR6CONR6; R6, R6a, R7 = independently H or aliph.; or N(R6)2 or N(R7)2 = independently heterocyclyl or heteroaryl; or C(R6a)2 = carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepd. I are protein kinase inhibitors, esp. of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 .mu.M: GSK-3.beta. (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases assocd. with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT **438203-20-4P 438203-23-7P 438203-25-9P**
438203-28-2P 438203-38-4P 438203-43-1P
438204-86-5P 438204-90-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-20-4 CAPLUS
CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)



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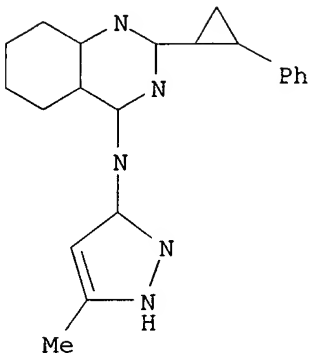

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L4 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:555487 CAPLUS
DOCUMENT NUMBER: 137:125169
TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3
INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Golec, Julian; Miller, Andrew; Knegtel, Ronald
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 333 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057259	A2	20020725	WO 2001-US49401	20011219
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WO 2002066461	A1	20020829	WO 2001-US49139	20011219
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WO 2002068415	A1	20020906	WO 2001-US50312	20011219

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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US 2003004161	A1	20030102	US 2001-26975		20011219
US 2003036543	A1	20030220	US 2001-25164		20011219
US 2003055068	A1	20030320	US 2001-26967		20011219
US 2003004164	A1	20030102	US 2001-34683		20011220
US 2003022885	A1	20030130	US 2001-34019		20011220
PRIORITY APPLN. INFO.:			US 2000-257887P	P	20001221
			US 2001-286949P	P	20010427

OTHER SOURCE(S): MARPAT 137:125169
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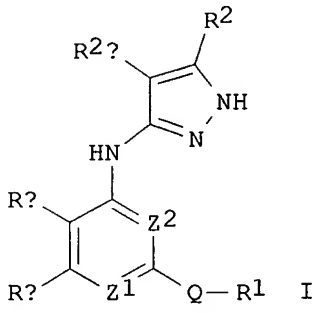

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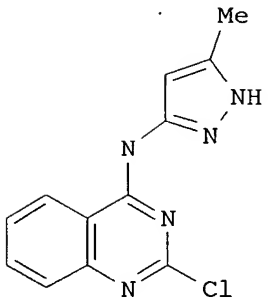

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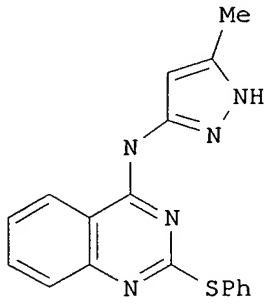


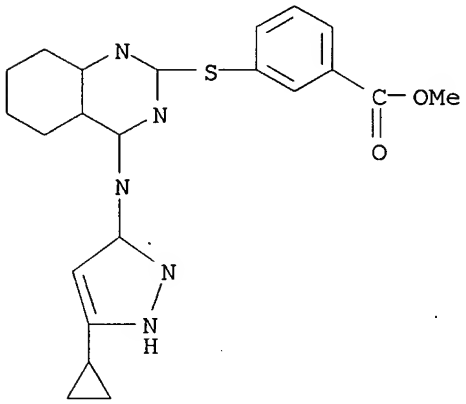
III

AB The title compds. I [Z1 = N, CR8; Z2 = N. CH; and at least one of Z1 and Z2 = N; Rb, Rc = TR3, LZR3; C2RbRc = (un)substituted fused (hetero)cycle; Q = NR4, O, S, etc.; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, carbocyclyl; T = a bond, alkylidene (un)interrupted by O, S, NR4, CO, etc.; Z = alkylidene; L = O, S, SO, SO2, etc.; R2, R2a = R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, etc.; R = H, (un)substituted aliph., (hetero)aryl, heterocyclyl; R4 = R7, COR7, SO2R7, etc.; W = CO, CO2, CONR6, etc.; R6, R7 = H, alkyl; or N(R6)2 or N(R7)2 = heterocyclyl, heteroaryl] were prepd.

For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in tert-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 .mu.M: GSK-3.beta. (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases assocd. with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

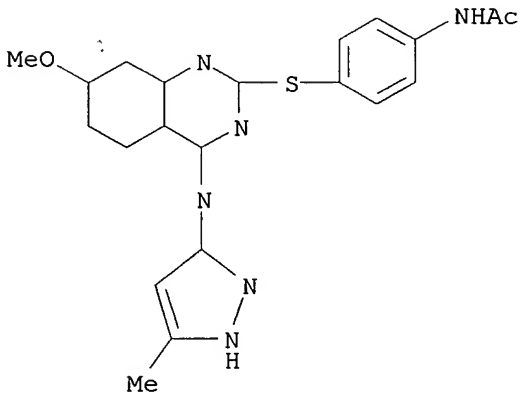
IT **438203-20-4P 438203-23-7P 438203-25-9P**
438203-28-2P 438203-38-4P 438203-43-1P
438204-86-5P 438204-90-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

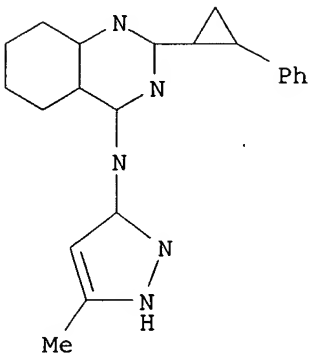
RN 438203-20-4 CAPLUS
CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 438203-23-7 CAPLUS
CN Acetamide, N-[4-[[7-methoxy-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]phenyl]- (9CI) (CA INDEX NAME)





*** FRAGMENT DIAGRAM IS INCOMPLETE ***

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:487556 CAPLUS
DOCUMENT NUMBER: 137:47221
TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer, diabetes, and Alzheimer's disease
INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Davies, Robert; Everitt, Simon; Kay, David; Knegtel, Ronald; Patel, Sanjay
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 342 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050065	A2	20020627	WO 2001-US49140	20011219
WO 2002050065	A3	20021024		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002034047	A5	20020701	AU 2002-34047	20011219
WO 2002066461	A1	20020829	WO 2001-US49139	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2002068415 A1 20020906 WO 2001-US50312 20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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US 2003004161 A1 20030102 US 2001-26975 20011219
US 2003036543 A1 20030220 US 2001-25164 20011219
US 2003055068 A1 20030320 US 2001-26967 20011219
US 2003004164 A1 20030102 US 2001-34683 20011220
US 2003022885 A1 20030130 US 2001-34019 20011220
PRIORITY APPLN. INFO.: US 2000-257887P P 20001221
US 2001-286949P P 20010427
WO 2001-US49140 W 20011219
OTHER SOURCE(S): MARPAT 137:47221

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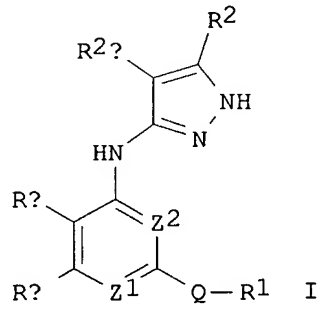

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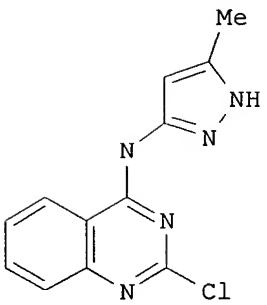

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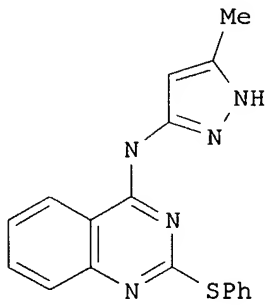


III

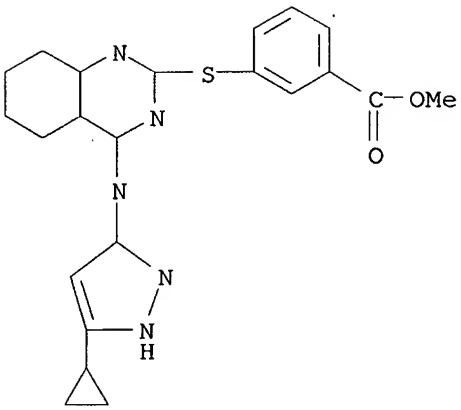
AB Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1 of Z1 and Z2 = N; Rx and Ry = independently TR3 or LZR3; or C2RxRy = (un)substituted fused (hetero)cycle; Q = NR4, O, S, C(6a)2, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D =

(un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, or carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4, CO, CONH, NHCO, SO2, SO2NH, NHSO2, CO2, OCO, OCONH, or NHCO2, with provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6, NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a = independently R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un)substituted aliph., (hetero)aryl, or heterocyclyl; R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2, CONR6, C(R6)2O, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or C(R6)2NR6CONR6; R6, R6a, R7 = independently H or aliph.; or N(R6)2 or N(R7)2 = independently heterocyclyl or heteroaryl; or C(R6a)2 = carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepd. I are protein kinase inhibitors, esp. of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 .mu.M: GSK-3.beta. (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases assocd. with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

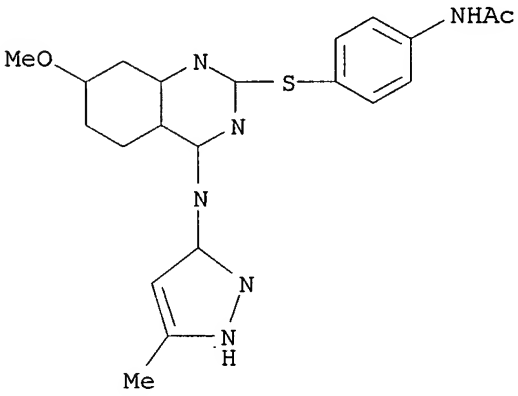
IT **438203-20-4P**, (5-Cyclopropyl-1H-pyrazol-3-yl)[2-(3-methoxycarbonylphenylsulfanyl)quinazolin-4-yl]amine **438203-23-7P**, [2-(4-Acetamidophenylsulfanyl)-7-methoxyquinazolin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-25-9P**, [2-(4-Acetamidophenylsulfanyl)-7-hydroxyquinazolin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-28-2P**, [2-(4-Acetamidophenylsulfanyl)-7-nitroquinazolin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-38-4P**, [2-(4-Acetamidophenylsulfanyl)-6-(4-methoxyphenyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-43-1P**, [6-Methoxycarbonyl-2-(4-propionylaminophenylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438204-86-5P** **438204-90-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-20-4 CAPLUS

CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 438203-23-7 CAPLUS
CN Acetamide, N-[4-[[7-methoxy-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]phenyl]- (9CI) (CA INDEX NAME)



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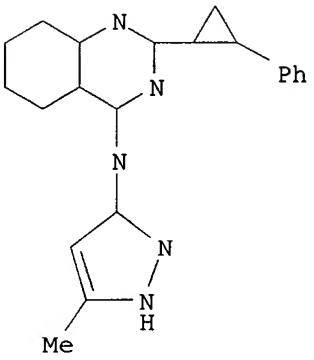

*** FRAGMENT DIAGRAM IS INCOMPLETE ***

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220584 CAPLUS
DOCUMENT NUMBER: 136:247584
TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease
INVENTOR(S): Bebbington, David; Knegtel, Ronald; Golec, Julian M. C.; Li, Pan; Davies, Robert; Charrier, Jean-Damien
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 356 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022608	A1	20020321	WO 2001-US42152	20010914
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AU 2001096871	A5	20020326	AU 2001-96871	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914

PRIORITY APPLN. INFO.:
US 2000-232795P P 20000915
US 2000-257887P P 20001221
US 2001-286949P P 20010427
WO 2001-US42152 W 20010914

OTHER SOURCE(S): MARPAT 136:247584
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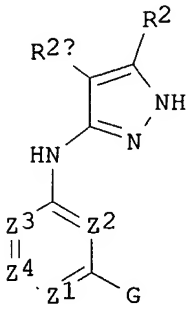

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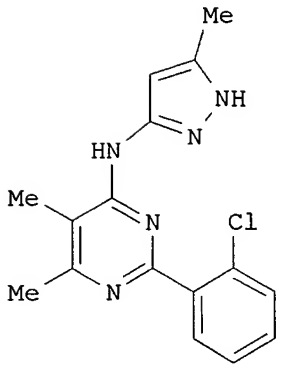


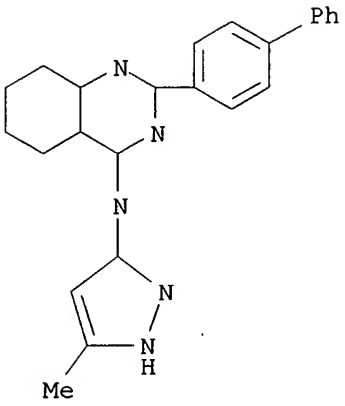
II

AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2S0-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliph.), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliph. group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 = CR9; Z2 and Z3 = N; Z4 = CRy]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-.beta.3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepd. and exhibited Ki values of < 0.1 .mu.M for glycogen synthetase kinase 3.beta. (GSK-3.beta.) and 0.1-1.0 .mu.M for Aurora-2.

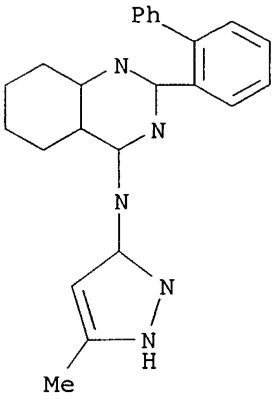
IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)
RN 404826-70-6 CAPLUS
CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220583 CAPLUS
DOCUMENT NUMBER: 136:247583
TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Davies, Robert; Bebbington, David; Knegtel, Ronald; Wannamaker, Marion; Li, Pan; Forester, Cornelia; Pierce, Albert; Kay, David
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 373 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022607	A1	20020321	WO 2001-US28940	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001091013	A5	20020326	AU 2001-91013	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914

PRIORITY APPLN. INFO.:
US 2000-232795P P 20000915
US 2000-257887P P 20001221
US 2001-286949P P 20010427
WO 2001-US28940 W 20010914

OTHER SOURCE(S): MARPAT 136:247583
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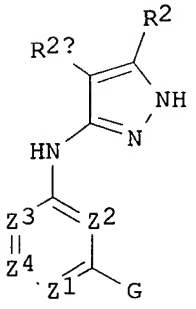

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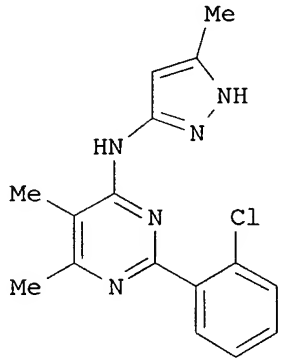

II

AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or

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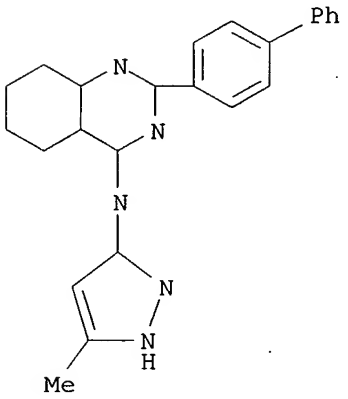
IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

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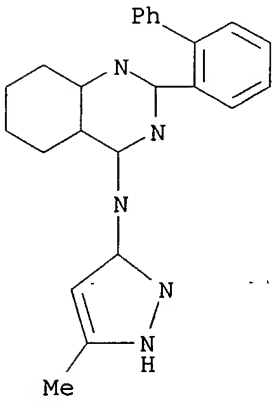
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes,

and Alzheimer's disease)
RN 404826-70-6 CAPLUS
CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



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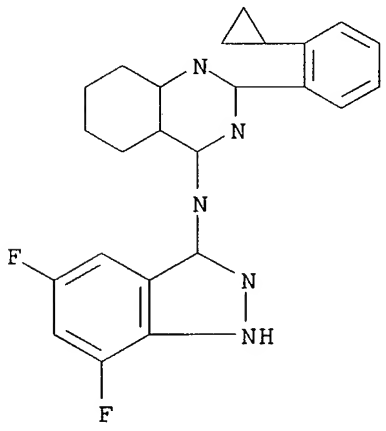

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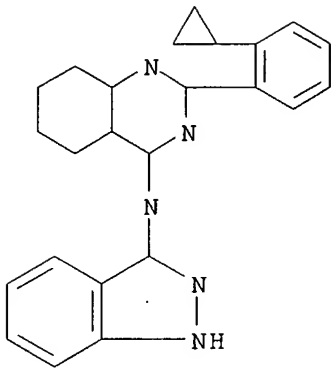

*** FRAGMENT DIAGRAM IS INCOMPLETE ***
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220582 CAPLUS
DOCUMENT NUMBER: 136:247582
TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease
INVENTOR(S): Bebbington, David; Binch, Hayley; Knegtel, Ronald; Golec, Julian M. C.; Patel, Sanjay; Charrier, Jean-Damien; Kay, David; Davies, Robert; Li, Pan; Wannamaker, Marion; Forster, Cornelia; Pierce, Albert
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 355 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022606	A1	20020321	WO 2001-US28803	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090944	A5	20020326	AU 2001-90944	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914

PRIORITY APPLN. INFO.:
US 2000-232795P P 20000915
US 2000-257887P P 20001221
US 2001-286949P P 20010427
WO 2001-US28803 W 20010914

OTHER SOURCE(S): MARPAT 136:247582
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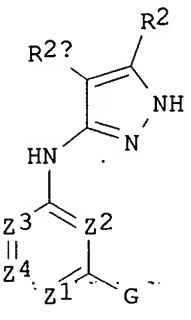

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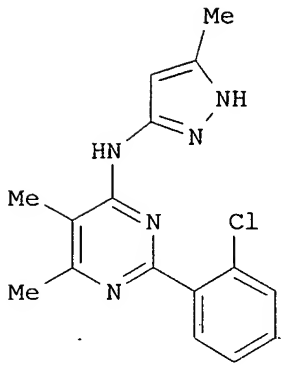

II

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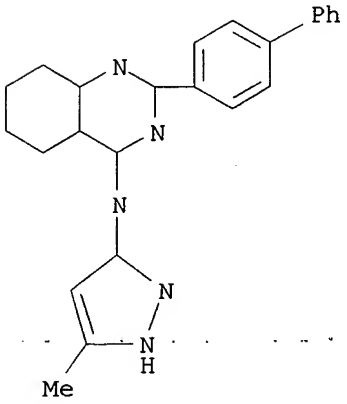
IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

IT **404826-70-6P,** (2-Biphenyl-2-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-70-6 CAPLUS

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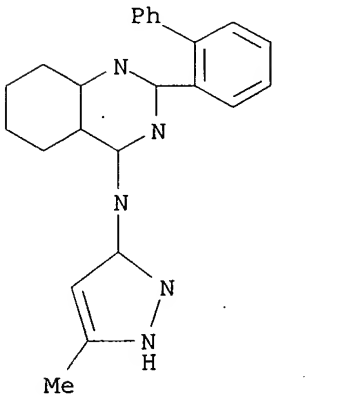


*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220581 CAPLUS

DOCUMENT NUMBER: 136:247581

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Golec, Julian M. C.; Charrier, Jean-Damien; Knegtel, Ronald; Bebbington, David; Davies, Robert; Li, Pan

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 357 pp.
CODEN: PIXXD2

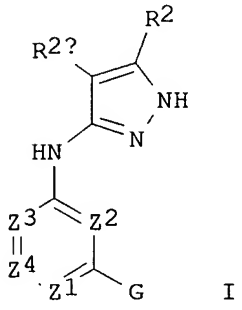
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022605	A1	20020321	WO 2001-US28793	20010914
W: AE, AG, AL, AM, AT, AU, AZ; BA, BB, BG, BR, BY, BZ, CA, CH, CN; CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001092670	A5	20020326	AU 2001-92670	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914

PRIORITY APPLN. INFO.:
US 2000-232795P P 20000915
US 2000-257887P P 20001221
US 2001-286949P P 20010427
WO 2001-US28793 W 20010914

OTHER SOURCE(S): MARPAT 136:247581

GI



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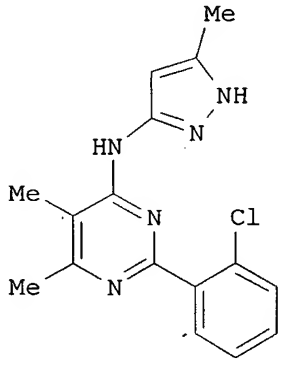


II

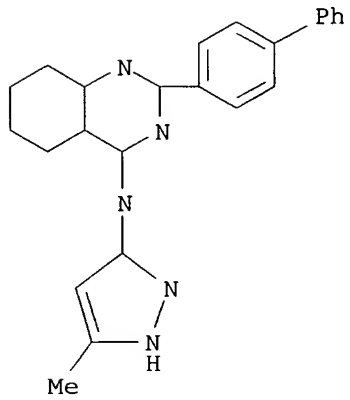
AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3

= N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2S0-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliph.), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliph. group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover pyrazolamines and indazolamines I [wherein Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N; at least one of Z1 or Z3 = N]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-.beta.3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepd. and exhibited Ki values of < 0.1 .mu.M for glycogen synthetase kinase 3.beta. (GSK-3.beta.) and 0.1-1.0 .mu.M for Aurora-2.

IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)

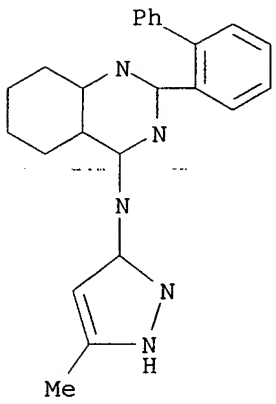


*** FRAGMENT DIAGRAM IS INCOMPLETE ***

IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-70-6 CAPLUS
CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220580 CAPLUS
DOCUMENT NUMBER: 136:247606
TITLE: Preparation of 3-(4-pyrimidinylamino)pyrazole derivatives as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treating cancer, diabetes and Alzheimer's disease.
INVENTOR(S): Davies, Robert; Bebbington, David; Binch, Haley; Knegtel, Ronald; Golec, Julian M. C.; Patel, Sanjay; Charrier, Jean-Damien; Kay, David; Davies, Robert
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 357 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022604	A1	20020321	WO 2001-US28792	20010914

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001094558	A5	20020326	AU 2001-94558	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914

PRIORITY APPLN. INFO.:
US 2000-232795P P 20000915
US 2000-257887P P 20001221
US 2001-286949P P 20010427
WO 2001-US28792 W 20010914

OTHER SOURCE(S): MARPAT 136:247606

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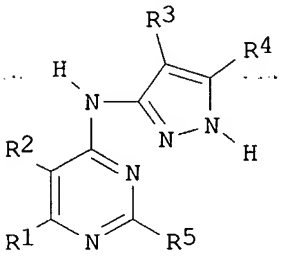

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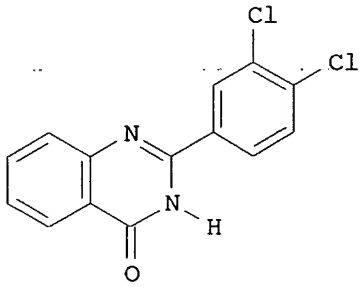

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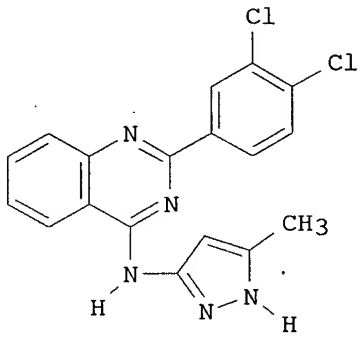


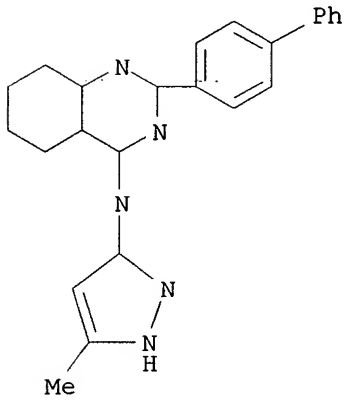
III

AB The prepn. of title compds. I and their pharmaceutically acceptable salts or prodrugs is described [wherein: R1, R2 = dependently form (un)substituted fused, unsatd. or partially unsatd., 5-8 membered carbocyclo ring; R3, R4 = independently H, aliph., aryl, heteroaryl, heterocyclyl, or wide variety of functionalized sidechains; or dependently form a fused, 5-8 membered, unsatd. or partially unsatd. ring having 0-3 ring heteroatoms (N, S, O); R5 = fused, (un)substituted 5-7 membered monocyclic ring or 8-10 membered bicyclic ring (aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms (N, S, O))]. For example, chlorination of quinazolone II with phosphorus oxychloride, followed by condensation with 3-amino-5-methylpyrazole afforded claimed compd. III. Compds. I are inhibitors of GSK-3 and Aurora-2 protein kinases. The invention also relates to methods of treating diseases assocd. with these protein kinases, such as diabetes, cancer and Alzheimer's disease. In bioassays, compds. I inhibited the following kinases with Kis reported < 100 nM: GSK-3.beta. (163 compds.), AURORA-2 (65 compds.), CDK-2 (no data), ERK2 (8 compds.), AKT (no data), and Human Src kinase (21 compds.). Claims

included 146 specific compds., and 188 examples were given. The syntheses of 6 compds. and 46 intermediates are described.

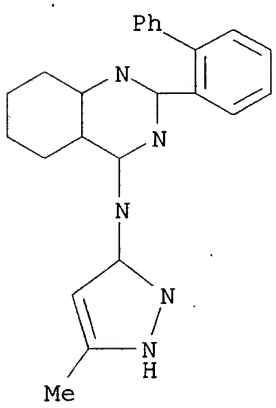
IT **404826-22-8P 404826-70-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-(4-pyrimidinylamino)pyrazole compds. as protein kinase inhibitors)

RN 404826-22-8 CAPLUS
CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 404826-70-6 CAPLUS
CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220579 CAPLUS

DOCUMENT NUMBER: 136:247580
TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease
INVENTOR(S): Davies, Robert; Li, Pan; Golec, Julian; Bebbington, David
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 406 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022603	A1	20020321	WO 2001-US28738	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090912	A5	20020326	AU 2001-90912	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914

PRIORITY APPLN. INFO.:
US 2000-232795P P 20000915
US 2000-257887P P 20001221
US 2001-286949P P 20010427
WO 2001-US28738 W 20010914

OTHER SOURCE(S): MARPAT 136:247580
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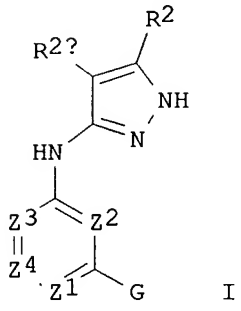

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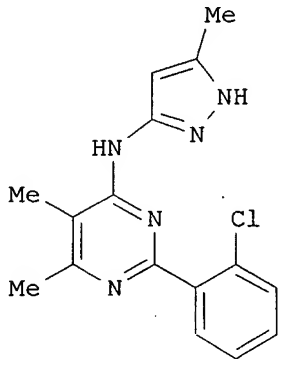


II

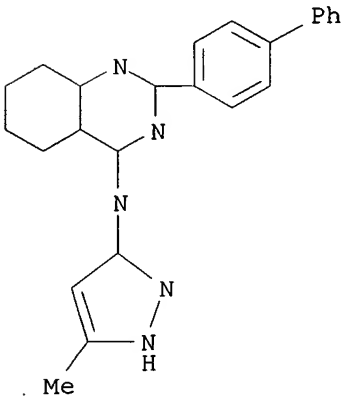
AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl,

heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SOO-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliph.), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliph. group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (triazinyl)pyrazolamines and indazolamines I [wherein Z1, Z2, and Z3 = N; Z4 = CRy]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-.beta.3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepd. and exhibited Ki values of < 0.1 .mu.M for glycogen synthetase kinase 3.beta. (GSK-3.beta.) and 0.1-1.0 .mu.M for Aurora-2.

IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



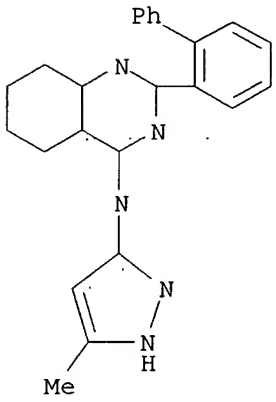
*** FRAGMENT DIAGRAM IS INCOMPLETE ***

IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-70-6 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220578 CAPLUS

DOCUMENT NUMBER: 136:263164

TITLE: Preparation of triazolamines as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Bebbington, David; Knegtel, Ronald; Binch, Haley; Golec, Julian M. C.; Li, Pan; Charrier, Jean-Damien

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 377 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022602	A2	20020321	WO 2001-US42162	20010914
WO 2002022602	A3	20020627		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001096875	A5	20020326	AU 2001-96875		20010914
US 2003055044	A1	20030320	US 2001-953505		20010914
PRIORITY APPLN. INFO.:			US 2000-232795P	P	20000915
			US 2000-257887P	P	20001221
			US 2001-286949P	P	20010427
			WO 2001-US42162	W	20010914

OTHER SOURCE(S): MARPAT 136:263164

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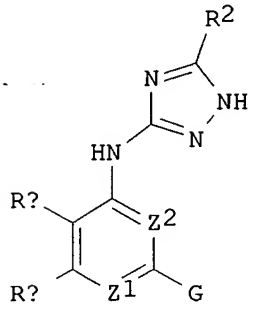

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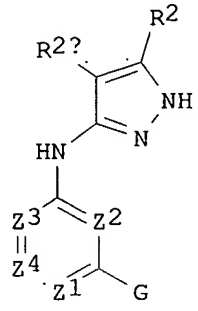

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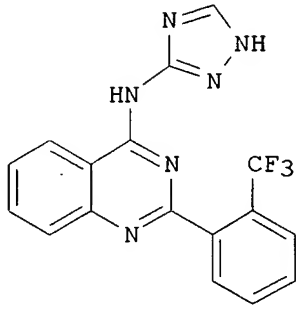


III

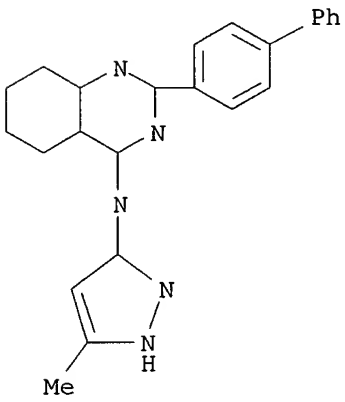
AB Triazolamines I and pyrazolamines II [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliph.), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliph. group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 =

R, halo, OR, COR, CO2R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (heterocyclyl)triazolamines I [wherein Z1 = N or CR9; Z2 = N or CH; R9 is defined above]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-.beta.3, Aurora-2, ERK, and Src. For instance, the N-(4-quinazolinyl)-1H-1,2,4-triazol-3-amine III was prepd. and exhibited Ki values of < 0.1 .mu.M for glycogen synthetase kinase 3.beta. (GSK-3.beta.) and 1.0-20 .mu.M for Aurora-2.

IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of triazolamines, pyrazolamines, and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)

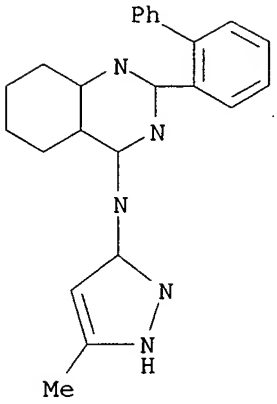


*** FRAGMENT DIAGRAM IS INCOMPLETE ***

IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; prepn. of triazolamines, pyrazolamines, and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-70-6 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



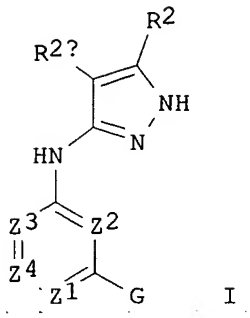
*** FRAGMENT DIAGRAM IS INCOMPLETE ***

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220577 CAPLUS
DOCUMENT NUMBER: 136:247579
TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease
INVENTOR(S): Knegtel, Ronald; Bebbington, David; Binch, Hayley; Golec, Julian; Patel, Sanjay; Charrier, Jean-Damien; Kay, David; Davies, Robert; Li, Pan; Wannamaker, Marion; Forster, Cornelia; Pierce, Albert
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 376 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022601	A1	20020321	WO 2001-US28740	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090914	A5	20020326	AU 2001-90914	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914

PRIORITY APPLN. INFO.:
US 2000-232795P P 20000915
US 2000-257887P P 20001221
US 2001-286949P P 20010427
WO 2001-US28740 W 20010914

OTHER SOURCE(S): MARPAT 136:247579
GI



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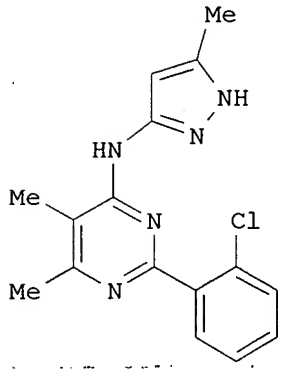
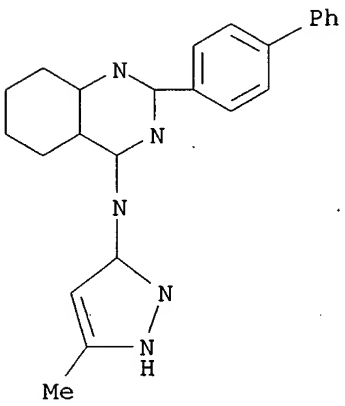


II

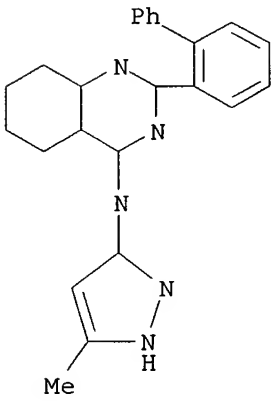
AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2S0-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliph.), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliph. group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover pyrimidinyl- and pyridinyl- pyrazolamines and indazolamines I [wherein Z1 = N, CRa, or CH; Z2 = N or CH; and at least one of Z1 or Z2 = N; Z3 = CRx; Z4 = CRy; Ra = halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, etc.; R and R4 are defined above]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-.beta.3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepd. and exhibited Ki values of < 0.1 .mu.M for glycogen synthetase kinase 3.beta. (GSK-3.beta.) and 0.1-1.0 .mu.M for Aurora-2.

IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS
CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl)(5-methyl-2H-pyrazol-3-yl)amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)
RN 404826-70-6 CAPLUS
CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

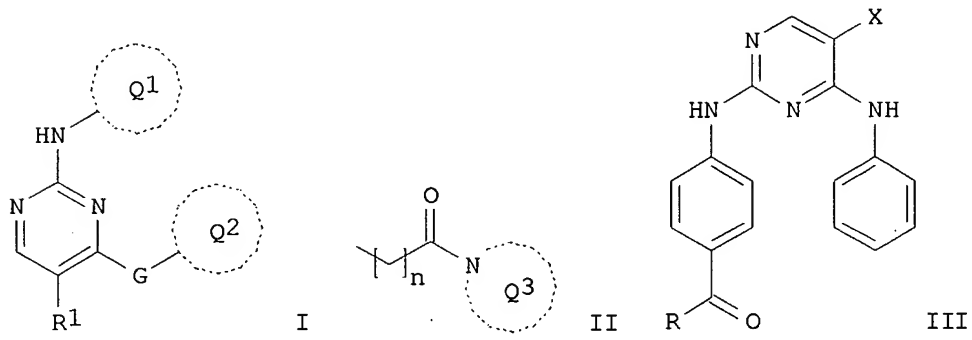
L4 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:661403 CAPLUS

DOCUMENT NUMBER: 135:227010
TITLE: Preparation of 2,4-di(hetero)arylamino(oxy)-5-substituted pyrimidines as antineoplastic agents
INVENTOR(S): Pease, Elizabeth Janet; Breault, Gloria Anne; Williams, Emma Jane; Bradbury, Robert Hugh; Morris, Jeffrey James
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064655	A1	20010907	WO 2001-GB824	20010226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2001008834	A	20021210	BR 2001-8834	20010226
EP 1268444	A1	20030102	EP 2001-906018	20010226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002004153	A	20021029	NO 2002-4153	20020830

PRIORITY APPLN. INFO.: GB 2000-4890 A 20000301
WO 2001-GB824 W 20010226

OTHER SOURCE(S): MARPAT 135:227010
GI



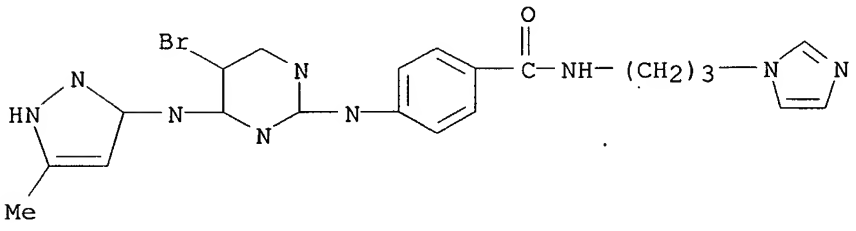
AB The title compds. [I; Q1, Q2 = (un)substituted aryl or carbon linked heteroaryl; and one or both Q1 and Q2 are substituted on a ring carbon by (CH2)nY(CH2)mZ or II (Y = NHCO, CONH; Z = (un)substituted cycloalkyl, Ph,

heterocyclyl, etc.; n = 0-1; m = 1-3; Q3 = (un)substituted nitrogen linked heterocycle); G = O, NR2; R2 = H, alkyl, alkenyl, etc.; R1 = H, halo, OH, etc.] and their pharmaceutically acceptable salts, useful as cyclin-dependent serine/threonine kinase (CDK) and focal adhesion kinase (FAK) inhibitors, were prepd. and formulated. Thus, reacting 4-anilino-2,5-dichloropyrimidine with 4-aminobenzoic acid followed by amidation of the resulting 4-anilino-2-(4-carboxyanilino)-5-chloropyrimidine with 1-(3-aminopropyl)imidazole afforded III [X = Cl; R = 3-(imidazol-1-yl)propylamino]. E.g., the title compd. III [X = Br; R = 2-(piperidino)ethylamino] showed IC50 of 0.235 .mu.M when tested in vitro assay for the CDK4 inhibitory activity.

IT **358789-01-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,4-di(hetero)arylamino(oxy)-5-substituted pyrimidines as antineoplastic agents)

RN 358789-01-2 CAPLUS

CN Benzamide, 4-[[5-bromo-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]amino]-N-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:617995 CAPLUS

DOCUMENT NUMBER: 135:180783

TITLE: Preparation of arylaminopyrimidines as Kinase inhibitors

INVENTOR(S): Armistead, David M.; Bemis, Jean E.; Di Pietro, Lucian V.; Geuns-Meyer, Stephanie D.; Habgood, Gregory J.; Kim, Joseph L.; Nunes, Joseph J.; Patel, Vinod F.; Toledo-Sherman, Leticia M.

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060816	A1	20010823	WO 2001-US4983	20010216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002052386 A1 20020502 US 2001-785599 20010216
US 20030004174 A9 20030102
EP 1257546 A1 20021120 EP 2001-909266 20010216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2000-183256P P 20000217
WO 2001-US4983 W 20010216

OTHER SOURCE(S): MARPAT 135:180783

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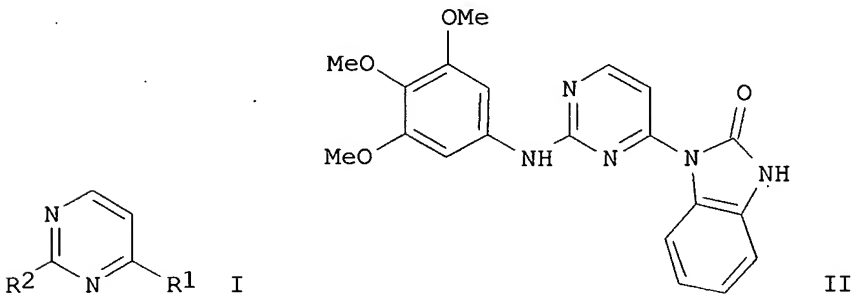


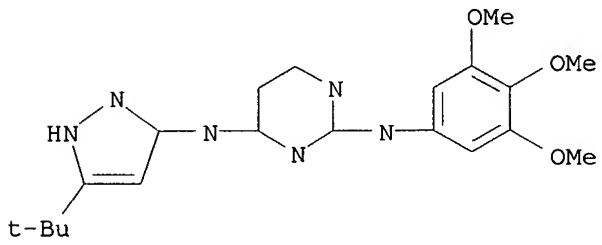
I II

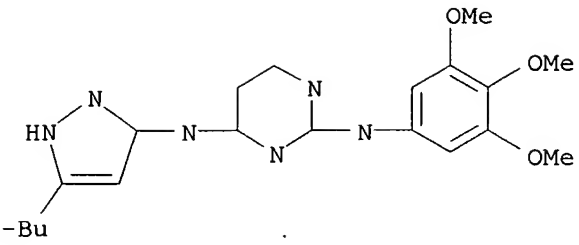
AB Arylaminopyrimidines I wherein R1 and R2 are independently aryl, 5-8 membered monocyclic, 11-14 membered bicyclic, 1-9-heteroatoms tricyclic, substituted amine, sulfide, alkoxy, acyl, heterocycle, were prepd. as Kinase inhibitors useful for treating disease or disease symptoms. Thus, pyrimidine II was prepd. and tested in vitro as kinases inhibitor (FGFR1-1, IC50 < 1.5 .mu.M).

IT **354817-37-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Prepn. of triazine Kinase inhibitors)

RN 354817-37-1 CAPLUS

CN 2,4-Pyrimidinediamine, N4-[5-(1,1-dimethylethyl)-1H-pyrazol-3-yl]-N2-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



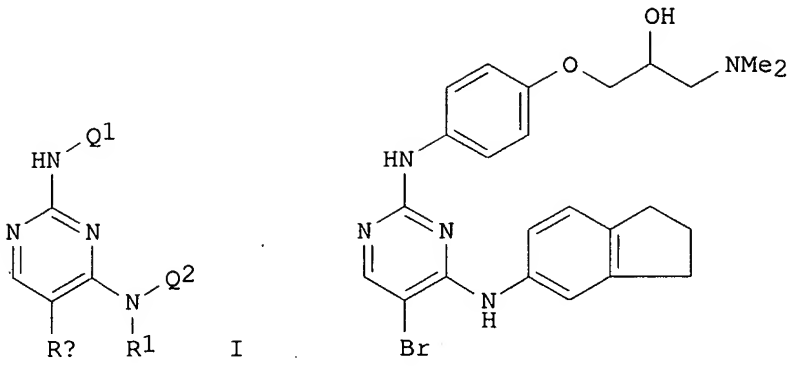


*** FRAGMENT DIAGRAM IS INCOMPLETE ***
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:457043 CAPLUS
DOCUMENT NUMBER: 133:89537
TITLE: Preparation of 2,4-pyrimidinediamine derivatives as anticancer agents
INVENTOR(S): Bradbury, Robert Hugh; Breault, Gloria Anne; Jewsbury, Philip John; Pease, Janet Elizabeth
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039101	A1	20000706	WO 1999-GB4325	19991220
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140860	A1	20011010	EP 1999-962375	19991220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916590	A	20011023	BR 1999-16590	19991220
JP 2002533446	T2	20021008	JP 2000-591012	19991220
NO 2001003038	A	20010822	NO 2001-3038	20010619

PRIORITY APPLN. INFO.: GB 1998-28511 A 19981224
WO 1999-GB4325 W 19991220
OTHER SOURCE(S): MARPAT 133:89537
GI



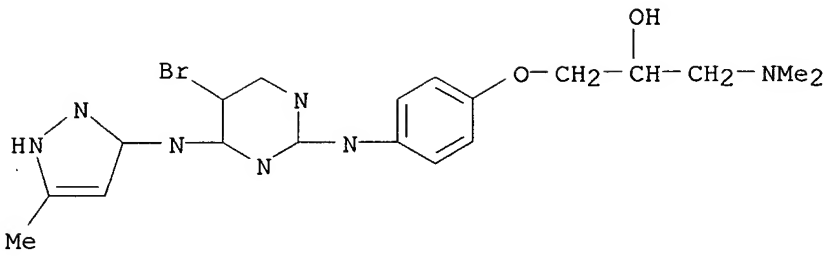
I II

AB The present invention relates to the title compds. (I) [wherein R1 = H, (un)substituted alkyl, alkenyl, or alkynyl, benzyl, 2-phenylethyl, phthalimidoalkyl, or cycloalkylalkyl; Rx = halo, OH, NO2, NH2, CN, SH, CO2H, SO2NH2, NHCHO, ureido, etc.; Q1 and Q2 = independently (un)substituted aryl, 5- or 6-membered monocycle, or 9- or 10-membered bicyclic heterocycle], processes for their manuf., and pharmaceutical compns. contg. them. For example, addn. of 4-[2-hydroxy-3-(N,N-dimethylamino)propoxy]aniline.bul.HCl in MeOH to 5-bromo-2-chloro-4-(indan-5-ylamino)pyrimidine in BuOH (prepns. given) and heating to 100.degree.C for 18 h gave II (42%). I inhibited the effects of cylin-dependent serine/threonine kinases (CDKs), showing selectivity for CDK2 (no data), CDK4 (IC50 ranging from 0.02 .mu.M to 0.07 .mu.M), and CDK6 (no data). In a tyrosine kinase activity assay using Sf21 cells transfected with plaque-pure FAK recombinant virus, I also inhibited focal adhesion kinase 3 (FAK3) with IC50 ranging from 0.032 .mu.M to 0.07 .mu.M. Typical IC50 values for I when tested for inhibition of cell growth in an Sulforhodamine B (SRB) assay were in the range of 1 mM to 1 nM. Thus, I possess anti-cancer properties, including anti-cell-migration, antiproliferation and/or apoptotic properties. Such properties are expected to be of value in the treatment of disease states assocd. with aberrant cell cycles and cell proliferation such as cancers (solid tumors and leukemias), fibroproliferative and differentiative disorders, psoriasis, rheumatoid arthritis, Kaposi's sarcoma, hemangioma, acute and chronic nephropathies, atheroma, atherosclerosis, arterial restenosis, autoimmune diseases, acute and chronic inflammation, bone diseases, and ocular diseases with retinal vessel proliferation.

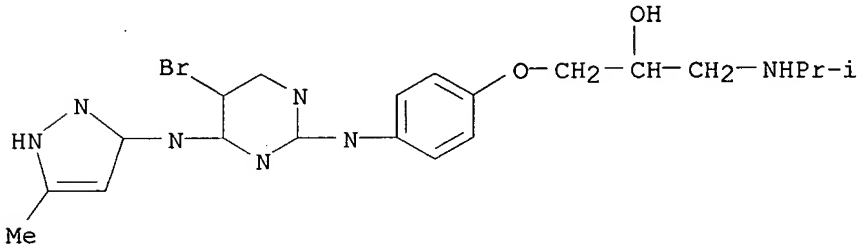
IT **280580-25-8P 280580-63-4P 280580-64-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,4-pyrimidinediamine anticancer agents by coupling halopyrimidines with anilines and optional derivatization)

RN 280580-25-8 CAPLUS

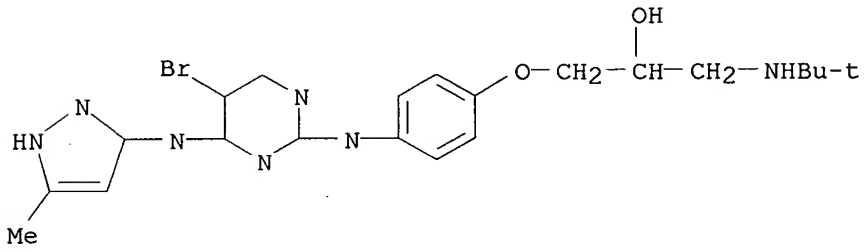
CN 2-Propanol, 1-[4-[[5-bromo-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]amino]phenoxy]-3-(dimethylamino)- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 280580-63-4 CAPLUS
CN 2-Propanol, 1-[4-[[5-bromo-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]amino]phenoxy]-3-[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 280580-64-5 CAPLUS
CN 2-Propanol, 1-[4-[[5-bromo-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]amino]phenoxy]-3-[(1,1-dimethylethyl)amino]- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	68.87	217.23

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.77	-9.77

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